REMARKS

This paper is submitted in response to the Final Office Action mailed May 19, 2004. Claims 50-99 are pending. Claims 50, 65-75 and 88-93 have been amended, as will be discussed in detail below. Support for amendments can be found throughout the specification and claims as originally filed, in particular in Table 1 at page 52, Table 4 at page 56 and page 25, line 24 to page 26, line 11. Since support for the amendments and new claims can be found throughout the specification and claims as originally filed, there is no new matter added as a consequence of the amendments or new claims. Applicants reserve the right to continue prosecution of cancelled subject matter in continuation or divisional applications.

The specification has also been amended to remove the incorporation by reference language, as requested by the Examiner.

The Rejections under 35 U.S.C. § 112 Should Be Withdrawn

Claims 88-99 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in a way as to reasonably convey to one skilled in the art that the inventors, at the time of the invention, had possession of the claimed invention. The Examiner alleges that there is no support for the sequences set forth in SEQ ID NOS: 13-18. The Examiner alleges that one of skill in the art would not readily recognize a genus of sequences based upon a couple of examples without some guidance as to which particular sequences are important for activity. The Examiner contends that the attempt to claim new sequences based on parts of already disclosed sequences is allegedly adding to the scope of the claimed invention. Without a statement or guidance to direct one of skill in the art to select any protein having rudimentary

identity to the claimed sequences, the Examiner alleges that the attempt to claim proteins of expanded scope is deemed new matter.

Applicants respectfully disagree with the Examiner's contention that the specification lacks guidance as to which sequences are important for activity. The specification clearly discusses the importance of specific motifs that confer antagonistic activity (specification, page 25, line 18 to page 26, line 11). The triple lysine motif and the QELD are specifically named as important sequences. The specification also describes the spatial orientation of the two motifs relative to each other (specification, page 25, line 25). The specification also notes that all the discussed toxins, SEA, SEB, SEC1, SEC2, SPEA and SEE contain at least the motifs, KK and QELD (specification, page 26, line 6-9). Therefore, Applicants submit that the specification provides clear guidance that specific motifs are important for the antagonistic activity of the peptide of the present invention.

Applicants also assert that it is within the knowledge of one of skill in the art to detect sequences in an alignment of various sequences that exhibit common or substantially identical residues at the same positions, for example, substantially identical residues in terms of polarity, charge and hydrophobicity, such as SEQ ID NOS: 13-18. These sequences, also known as consensus sequences, are the average or most typical form of a sequence that is reproduced with minor variations in a group of related DNA, RNA or amino acid sequences, showing the nucleotide or amino acid most often found at a particular position in the sequence. Their presence also implies an important activity shared by all molecules that possessing them. Applicants assert that one of skill in the art would easily detect the consensus sequences of the present invention and recognize that the inventors were in possession of the claimed invention.

As indicated in the prior Amendment mailed February 11, 2004, SEQ ID NOS: 13-18 are clearly derived from the sequences set forth in SEQ ID NOS:1-11. SEQ ID NOS: 13, 14 and 15 are derived directly from sequences listed at positions 152-161 and position 152-161* of Table 1. SEQ ID NOS: 16, 17 and 18 are derived from sequences listed at position 150-161 and position 150-161*. The listed sequences on Table 1 are even arranged so that the shared positions that form the consensus sequence are aligned. Applicants submit that these common motifs would be obvious to one of skill in the art, upon review of the sequences listed in Tables 1 and 4. Taken together with the guidance found in the specification regarding antagonistic activity of specific motifs, Applicants submit that the specification provides sufficient description for one of skill in the art to conclude that the inventors had possession of the claimed invention at the time of the invention. Therefore, Applicants assert that the specification discloses sufficiently detailed, relevant characteristics which provide evidence that the Applicant was in possession of the claimed invention with regard to claims 88-99.

In addition, the Examiner has rejected claims 65-75 and 88-99 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in a way as to reasonably convey to one skilled in the art that the inventors, at the time of the invention, had possession of the claimed invention. The Examiner contends that the genus is highly variant and there is insufficient support for describing the genus. The Examiner also contends that SEQ ID NOS: 1-11 and 13-18 are insufficient to describe the genus and that the specification lacks the description of a function shared by the 10 amino acid fragments. In particular, the Examiner alleges that the antagonistic activity is drawn only from two sequences and that the antagonistic activity "may" only be associated with the two sequences. The Examiner further assert that the presumption of

activity on a fragment of a protein compared between two sequences allegedly does not rise to the level of providing support for the genus of claims "comprising" fragments of proteins.

Applicants respectfully disagree and continue to assert that the specification provides sufficient number of representative species and the function shared by the members of the genus to support a claim using the "comprising" language. An applicant may show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e. complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. *Guidelines for Examination of Patent Application Under the 35 U.S.C., ¶1, "Written Description" Requirement.* 66 FR 1099, 1106. Applicants submit that the specification provides the partial structure of the specified sequences, as well as the functional characteristic of antagonistic activity.

However in the interest of furthering prosecution, Applicants have amended claims 65-75 and 88-99 to recite "consisting of" instead of "having." Applicants further submit that the claims, as amended, contain subject matter which is clearly described as to reasonably convey to one skilled in the art that the inventors, at the time of the invention, had possession of the claimed invention.

For the foregoing reasons, Applicants respectfully request the withdrawal of the rejections of claims 65-75 and 88-99.

The Rejections under 35 U.S.C. § 102 Should Be Withdrawn

Claims 50-65, 68, and 76-87 are rejected under 35 U.S.C. § 102(b) as being anticipated by Tice et al. (US 5,407,609). The Examiner alleges that Tice et al. disclose a formalinized staphyloccal enterotoxin (SEB) molecule that does not exhibit toxin agonist activity and allegedly has features homologous to the features recited in the instant claims. The Examiner alleges that the claimed peptide needs only to be similar (homologous) to one which has the recited limitations of the claims. Given that the primary amino acid sequences of the SEB disclosed by Tice et al. and the SEB of the present invention are identical, the Examiner further alleges that the recited limitation has been met. Applicants respectfully disagree.

Claim 50 has been amended to recite an isolated and purified peptide *consisting of* an amino acid sequence homologous to an amino acid sequence of a domain of a pyrogenic exotoxin having the specific claimed structure, wherein said isolated peptide does not have toxin agonist activity and is capable of antagonizing toxin-mediated activation of T lymphocytes. The claimed peptide consists of the antagonist domain which forms a central turn in the toxin molecule, where the domain consists of starting within β- strand 7 and connecting the β- strand 7, via β- strand 8, to α- helix 4, and ending within α-helix 4 (based on the numbering of SEB). Furthermore, according to the description of Figure 2 (page 10, lines 18-28), the β- strand 7 structure in SEB encompasses residues 141-151, the β-strand 8 includes residues 154-156 and the α-helix 4 contains residues 157-172. The antagonist domain is limited to a peptide no longer than the amino acid residues 141-172 of SEB. Therefore, amended claim 50 now relates to the isolated and purified peptide consisting of an antagonistic domain.

Tice et al. fails to recite each and every limitation of the presently claimed invention. In particular, the chemically-modified structure of the full-length SEB protein, which has been

treated by formalin, is not limited to consisting of the above-cited antagonistic structural domain of the present invention.

It should be further noted that the term "homologous" is well-defined in the specification as to the claimed peptides, and those skilled in the art would be able to ascertain the metes and bounds of the claims. For example, page 25, line 18 to page 26, lines 11-32, discusses sequence homologies between related pyrogenic toxins in the domain of such toxins that forms the "central turn" of the molecules, corresponding to amino acids 150-161 of SEB. The specification clearly provides that KKK and QELD motifs are common to SEB, as well as to the related toxins, SEA, SEC1, SEC2, SPE A. The domain is highly conserved among the exotoxins in this family. Indeed, the related exotoxin proteins share between 9 out of 12 to 10 out of 12 amino acid residues with SEB in the region of amino acids 150-161 of SEB (in the central turn domain) See, e.g. Example 2 page 36 and Example 6, page 41, lines 1-13. The use of the term "homologous" in the context as applied in the specification and claim correlates to a high degree of identity of amino acids in the claimed antagonistic domain. Mere "similarity" (as alleged by the Examiner) to the sequences of the claimed structure is inconsistent with a reading of the specification. Since the specification sets forth an interpretation for the use of the term "homologous" that requires a high degree of identity of sequences in the domain, Applicants assert that the peptide of Tice et al. cannot anticipate the presently claimed peptide.

Furthermore, Tice et al. fails to disclose a peptide that is *capable of antagonizing toxin-mediated T-lymphocyte activation*, i.e. inhibition of SEB and other toxins, such as SEA, TSST-1 to mediate induction of IL-2, IFN-γ and/or TNF-β gene expression. Tice et al. does not test or present full-length or fragments of SEB as having the requirements of the presently

claimed peptides. For this additional reason, Applicants submit that Tice et al. cannot anticipate claims 50-65, 68, and 76-87 of the present invention.

Claims 89-90, 92-93, 95, 96, 98 and 99 are rejected under 35 U.S.C. § 102(b) as being anticipated by Ratti et al. The Examiner alleges that Ratti et al. discloses a protein encoded by ORF6D having sequences identical to those derived from *Chlamydia trachomatis*. The Examiner alleges that Ratti et al. discloses a peptide with the identical structural requirements set forth in SEQ ID NOS:14 or 17. The Examiner further allege that the inhibitory activity is an inherent activity imparted to the structure of the molecule.

In contrast to the present invention, the molecule of Ratti et al. fails to disclose a peptide *consisting of* an amino acid sequence homologous to an amino acid sequence of a domain of a pyrogenic exotoxin having the presently claimed structure, wherein said isolated peptide does not have toxin agonist activity and is capable of antagonizing toxin-mediated activation of T lymphocytes. Therefore, Applicants submit that Ratti et al. cannot anticipate claims 89-90, 92-93, 95, 96, 98 and 99 of the present invention.

In addition, claims 88 and 94 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Galinski et al. The Examiner alleges that Galinski et al. disclose a polymerase-associated nucleocapsid phosphoroprotein obtained from parainfluenze virus, which meets the structural requirements set forth in SEQ ID NO: 13. The Examiner further allege that the antagonistic activity is an inherent activity imparted to the structure of the molecule.

For the reasons stated above, Applicants submit that Galinski et al. cannot anticipate the claims of the present invention. Galinski et al. fail to exhibit the capability of antagonizing toxin-mediated activation of T lymphocytes and do not mention any sequence or peptide isolated that is capable of inhibiting SEB or other toxins, e.g. SEA and TSST-1, to mediate the activation

of IL-2, IFN-γ and TNF-β. The molecule of Galinski et al. also fails to disclose a peptide *consisting of* an amino acid sequence homologous to an amino acid sequence of a domain of a pyrogenic exotoxin having the presently claimed structure. Therefore, Galinksi et al. cannot anticipate claims 88 and 94.

Furthermore, claims 91 and 97 has been rejected under 35 U.S.C. § 102(b) as being anticipated by Spriggs et al. The Examiner alleges that Spriggs et al. disclose a polymerase-associated nucleocapsid phosphoroprotein obtained from parainfluenza virus, which meets the structural requirements set forth in claims 91 and 97.

Similar to the cited art described above, the peptide of Spriggs et al. fails to exhibit the capability of antagonizing toxin-mediated activation of T lymphocytes. In addition, Spriggs et al. do not mention any sequence or peptide isolated is capable of inhibiting SEB or other toxins, e.g. SEA and TSST-1, to mediate the activation of IL-2, IFN-γ and TNF-β. The molecule of Spriggs et al. also fails to disclose a peptide *consisting of* an amino acid sequence homologous to an amino acid sequence of a domain of a pyrogenic exotoxin having the presently claimed structure. Therefore, Applicants submit that Spriggs et al. cannot anticipate claims 91 and 97 of the present invention.

For the foregoing reasons, Applicants respectfully request the withdrawal of the rejection of the claims and reconsideration of the pending claims.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully request withdrawal of the outstanding rejections and allowance of the pending claims.

Applicants do not believe that any additional fee is required in connection with the submission of this document. However, should any fee be required, or if any overpayment has been made, the Commissioner is hereby authorized to charge any fees, or credit or any overpayments made, to Deposit Account 02-4377. A duplicate copy of this sheet is enclosed.

Respectfully submitted,
BAKER BOTTS LLP

Rochelle K. Seide
Patent Office Reg. No. 32,300

Carmella L. Stephens
Patent Office Reg. No. 41,328

Attorneys for Applicants

30 Rockefeller Plaza
New York, NY 10112-4498
(212) 408-2500